IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

ERFINDERGEMEINSCHAFT UROPEP GbR, Plaintiff, v. ELI LILLY AND COMPANY, and BROOKSHIRE BROTHERS, INC., Defendants.	)	CASE No. 2:15-cv-01202-WCB

PLAINTIFF UROPEP'S MOTION FOR CONFIRMATION OF THE COURT'S CLAIM CONSTRUCTION ORDER AND PARTIAL SUMMARY JUDGMENT OF INFRINGEMENT AND MEMORANDUM OF LAW IN SUPPORT THEREOF

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INTRODUCTION

Lilly infringes UroPep's '124 patent. The '124 patent claims a method for treating benign prostatic hyperplasia ("BPH") by administering phosphodiesterase type 5 ("PDE5") inhibitors in an effective amount. Despite its knowledge of the '124 patent, Lilly encourages doctors to prescribe its PDE5 inhibitor Cialis for treatment of BPH, and encourages patients to take Cialis for BPH. Lilly thus induces infringement as a matter of law.

Faced with overwhelming evidence of infringement, Lilly generates two unpersuasive non-infringement arguments. First, Lilly argues that Cialis does not treat BPH because it only treats the signs and symptoms of BPH. But treating the signs and symptoms of BPH is a way to treat BPH. Lilly's little word play is nothing more than a new claim construction argument and runs contrary to (1) the specification, (2) Lilly's own admissions to the patent office, (3) the applicable clinical guidelines at the time of the invention, and (4) the scientific literature.

Second, Lilly engages in a counterfactual and erroneous over-reading of the Court's claim construction to create last-ditch invalidity and non-infringement arguments. This Court construed "an inhibitor of phosphodiesterase (PDE) V" and, on UroPep's urging, incorporated a selectivity requirement. As the Court noted, that selectivity limitation came from the prosecution of the parent '061 patent, U.S. Patent No. 8,106,061, wherein the use of the compounds in the Heiker reference to treat diseases was distinguished. The Heiker compounds inhibited PDE5 as well as PDE1 and PDE2, and so UroPep stated that its invention was the use of "selective" inhibitors of PDE5 – i.e. inhibitors of PDE5 that did not also inhibit PDE1 or PDE2, like those in Heiker did. And read in the context of the specification, which mentions only five families of PDEs (PDE1-5), a "selective" PDE5 inhibitor is one that inhibits PDE5 20 times more than it does PDEs 1-4.

Lilly ignores this context, misinterpreting the phrase "all other specific PDEs" in the Court's claim construction ruling to argue that this includes PDE6 (and PDE7 – PDE11) even though PDE6 is unmentioned in the '124 patent specification and was not the basis on which the compounds of the prior art were distinguished. Lilly does this in part because none of the example compounds of the '124 patent inhibit PDE5 20 times more than PDE6. Indeed, there were zero reports of any PDE5 inhibitor that did so as of July 1997 when it was thought that all PDE5 inhibitors also inhibited PDE6. Lilly's over-reading of this Court's order is plainly incorrect, as it invariably leads to the conclusion that the '124 patent claims cover zero of the preferred embodiments listed in the specification (because none are 20 times selective for PDE5 over PDE6). *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) (construction where specification's only embodiment falls outside the scope of the patent claim is "rarely, if ever, correct"). The Court did not construe the claims in a way at odds with the intrinsic record or in a manner designed to invalidate the '124 patent and end the case.

Lilly takes this argument one step further and asserts that tadalafil is also not "selective" under the Court's construction because it is less than 20 times more selective for PDE5 than PDE11. But PDE11 is not one of the five PDEs mentioned in the '124 patent specification, and was not one of the PDEs that were the subject of the Heiker prior art upon which this entire "selective" requirement rests. In fact, PDE11 was not discovered as of July 1997 and therefore no method would have existed to determine selectivity against PDE11 at that time.

Disclaimers distinguish the prior art from the pending claims. Claims should not be construed to exclude all the embodiments of a specification and to render a patent invalid. And claims cannot be construed such that infringement is to be measured using tools that did not even exist as of the priority date. *Raybestos-Manhattan, Inc. v. Texon, Inc.*, 268 F.2d 839, 842 (1st

Cir. 1959 (tests for non-infringement must have been "employed at the time of the patent application . . . by a person skilled in the art.").

Summary judgment is particularly appropriate here because Lilly's non-infringement arguments depend fundamentally on its misinterpretation of key claim terms. Lilly's first argument – that Cialis does not "treat" BPH – is based on Lilly's misreading of the claim term "treatment." Similarly, Lilly's argument that tadalafil is not a "selective" inhibitor of PDE5 rests on its erroneous and enthusiastic misinterpretation of the Court's claim construction ruling. As the parties' only dispute regarding infringement boils down to a legal dispute over the meaning of the claims, there is no factual issue for the jury to decide. *O2 Micro Int'l, Ltd. v. Beyond Innovation Tech. Co., Ltd.*, 521 F.3d 1351, 1361-1362 (Fed. Cir. 2008). The Court should decide these issues as a matter of law and grant UroPep's motion for partial summary judgment.

I. STATEMENT OF THE ISSUE TO BE DECIDED

Does administration of Cialis (tadalafil) for BPH infringe claims 1 and 3 of the '124 patent, and does Lilly induce that infringement?

II. STATEMENT OF UNDISPUTED MATERIAL FACTS

The USPTO awarded UroPep the '124 patent in July 2014. Ex. 1, '124 Pat. The '124 patent claims a "method for prophylaxis or treatment of benign prostatic hyperplasia comprising administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V, excluding a compound selected from the group consisting of [a group of nine compounds]."[1] *Id*. at claim 1. Tadalafil is not one of the excluded compounds. *Id*. The patent also claims a "method of claim 1 wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form." *Id*. at claim 3.

[1] Phosphodiesterase type 5 can be referred to as either "PDE V" or "PDE5."

According to the Court's construction, a PDE5 inhibitor is "a compound that selectively inhibits PDE5"; that is, a compound that is "at least 20 times more effective in inhibiting [PDE5] as compared to all other specific PDEs." Order 10/21/16 (Dkt. 149) at 27. The '124 patent itself, which has a priority date of July 9, 1997, identifies the relevant specific PDEs as PDEs 1-5. Ex. 1, '124 Pat., Col. 1, ll. 60-63 (referencing "five different sPDEs which are differently distributed in the individual organs"). Two other PDEs were known at the time – PDE6 and PDE7. *See* Ex. 2, Beavo 1 Rep., ¶ 15; Ex. 3, Beavo Responsive Rep., ¶ 9. But PDE6 was known only to be in the retina (not the prostate), and PDE7 had not been identified in any specific human tissue. *See* Ex. 4, Bell Rep. ¶¶ 17-18; Ex. 5, Beavo 1995 at 740. Other PDEs, including PDE11, were not discovered until later. *See* Ex. 2, Beavo 1 Rep. ¶¶ 15-17.

Tadalafil "is a phosphodiesterase 5 (PDE5) inhibitor indicated for the treatment of . . . the signs and symptoms of benign prostatic hyperplasia (BPH)" and "ED and the signs and symptoms of benign prostatic hyperplasia." Ex. 6, Cialis label at 1. Further, tadalafil is "a selective inhibitor of . . . PDE5," and "is >10,000-fold more potent for PDE5" than for the other PDEs referenced in the patent, namely, PDE1, PDE2, PDE3, and PDE4. *Id*. at 11-12.

Lilly has heavily marketed Cialis for BPH and BPH + ED. For example, Lilly's sales reps meet with doctors and provide them promotional materials that encourage them to prescribe Cialis for patients with BPH or ED plus BPH. Ex. 7, Sliwinski Rep. ¶¶ 42-44, Ex. 7 ("Is your erectile dysfunction (ED) patient living with benign prostatic hyperplasia (BPH) symptoms? Two conditions. One treatment. **Cialis 5 mg for once daily use**."). Other marketing is directed to end users of Cialis, encouraging them to take Cialis for BPH or BPH + ED. Doctors are frequently asked for Cialis by name (or by reference to the "bathtub drug," which references a well-known Cialis ad with couples sitting in bathtubs). Ex. 7, Sliwinski Rep. ¶ 47.

Lilly has known about the '124 patent since receiving a letter informing it that selling Cialis for BPH required a license to the '124 patent. Ex. 8, Oct. 9, 2014 Notice Letter. Lilly never responded, nor did it cease efforts to encourage others to directly infringe the '124 patent.

III. ARGUMENT

Under the Court's claim construction there is no genuine fact dispute that administering Cialis for BPH infringes the '124 patent. And the undisputed material facts demonstrate that Lilly has induced this infringement. Summary judgment is appropriate where there is no genuine dispute as to any material fact. *Solvay S.A. v. Honeywell Int'l, Inc.*, 622 F.3d 1367, 1373 (Fed. Cir. 2010); Fed. R. Civ. P. 56(a). Summary judgment is especially appropriate here, because Lilly's non-infringement arguments turn solely on a claim construction issue: the meaning of the terms "treatment" and "selective." *O2 Micro*, 521 F.3d at 1361-62.

To prove inducement, the patentee must "show direct infringement, and that the alleged infringer 'knowingly induced infringement and possessed specific intent to encourage another's infringement.'" *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1363 (Fed. Cir. 2012) (internal citations omitted). "Direct infringement [of a method claim] occurs only when someone performs the claimed method." *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 850 (Fed. Cir. 2010). A party induces infringement when it encourages another party to infringe. *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1305 (Fed. Cir. 2006). An accused infringer has the intent to encourage infringement when it knows of the patent and that the induced acts constitute patent infringement. *Commil USA, LLC v. Cisco Sys., Inc.*, 135 S. Ct. 1920, 1926 (2015).

A. Direct infringement

The '124 patent claims in relevant part a "method for prophylaxis or treatment of [BPH] comprising administering to a person in need thereof an effective amount of an inhibitor of

phosphodiesterase (PDE) V . . . ." Ex. 1, '124 Pat. at claim 1. Physicians and patients directly infringe the patent because (1) administering tadalafil for BPH is a method for prophylaxis or treatment of BPH, (2) tadalafil is an inhibitor of PDE5, and (3) prescribing or taking Cialis for BPH comprises administering tadalafil to a person in need thereof in an effective amount.

1. Administering Cialis is a method for the prophylaxis or treatment of BPH

Cialis is indicated both "for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH)" and "for the treatment of ED and the signs and symptoms of BPH (ED/BPH)." Ex. 6, Cialis label at 2. Physicians prescribe Cialis for, and patients take Cialis as, a treatment and prophylaxis for BPH and BPH + ED. Ex. 7, Sliwinski Rep. ¶¶ 48-49.

Lilly's first non-infringement position comes from limiting "treatment of BPH" to shrinking or slowing the growth of the prostate. Ex. 9, Roehrborn Rep. ¶ 84; Ex. 10, Roehrborn Rebuttal Rep. ¶ 18. Under Lilly's narrow approach, the only medication that "treats" BPH is a 5-alpha reductase inhibitor ("5ARI"). Ex. 9, Roehrborn Rep. ¶ 84; Ex. 10, Roehrborn Rebuttal Rep. ¶¶ 22-23. Lilly's limited construction is belied by the specification, Lilly's admissions, the scientific literature, and physicians' understanding of the treatment of BPH.

First, the '124 patent specification explains that "medicament treatments" for BPH included "alpha-receptor blockers." Ex. 1, '124 Pat., Col. 1, ll. 24-31. UroPep and Lilly experts agree that alpha-blockers do not shrink the size of the prostate, but rather, like PDE5 inhibitors, relax smooth muscle. Ex. 10, Roehrborn Rebuttal Rep. ¶¶ 19-20; Ex. 11, Kaplan Rebuttal Rep. ¶¶ 35-36. The specification also explains that the "excellent efficiency in the treatment of prostatic diseases" achieved by administering PDE5 inhibitors results from the "relaxation of the prostatic muscles." Ex. 1, '124 Patent, Col. 2, ll. 12-16. The patent says nothing about shrinking the prostate nor has anyone ever postulated that PDE5 inhibitors could shrink the prostate.

Lilly's construction would mean no one could ever practice the claims of the '124 patent and is directly contrary to the specification.

Second, in claim 1 of a 2006 patent application in which Lilly sought to cover the administration of Cialis (tadalafil) for treating BPH, Lilly told the USPTO that tadalafil is a method of treating BPH in male mammals in need of such treatment. Ex. 12, U.S. Patent Application. No. 11/545,173 ("the '173 Application").[2] In claim 2 (which is dependent on claim 1), Lilly told the USPTO that one way Cialis treats BPH is to "reduce the frequency or severity of at least one symptom of BPH." *Id*. In other words, according to Lilly's '173 Application, tadalafil treats BPH, and treating the signs and symptoms of BPH *just is* a way to treat BPH.

Third, practice guidelines at the time demonstrate that treating symptoms of BPH is one way to treat BPH. For example, the Agency for Health Care Policy and Research's 1994 clinical practice guidelines explain that only one treatment shrinks the prostate (finasteride). Ex. 13, AHCPR Guidelines at 4-6, 67. *Id*. Other BPH treatments work by contracting prostatic smooth muscle (alpha blocker therapy) or stretching the urethra (balloon dilation). *Id*.

Lilly cites two product labels to support its argument that treating BPH is limited to shrinking the prostate or slowing prostate growth. Ex. 10, Roehrborn Rebuttal Rep. ¶¶ 19-23. One label is for FLOMAX, an alpha-blocker drug that does not shrink the prostate and is indicated for the "treatment of the signs and symptoms of benign prostatic hyperplasia." *Id*. at 20. The other label is for PROSCAR, a 5ARI drug that does shrink the prostate and is indicated for the "treatment of benign prostatic hyperplasia." *Id*. at 23. But these cherry-picked examples

[2] The '173 Application is titled "Treatment of Benign Prostatic Hypertrophy and Lower Urinary Tract Symptoms." Benign prostatic hypertrophy and benign prostatic hyperplasia are interchangeable. Ex. 12, the '173 Application ("Benign Prostatic Hypertrophy (BPH), also termed Benign Prostatic Hyperplasia….").

do not support the distinction Lilly tries to draw. Two more examples are helpful. The alpha-blocker drug HYTRIN is indicated for "the treatment of symptomatic benign prostatic hyperplasia." Ex. 14, HYTRIN label. The 5ARI drug AVODART is also indicated for "the treatment of symptomatic benign prostatic hyperplasia." Ex. 15, AVODART label. One medication shrinks the prostate, the other does not. But both are indicated for treatment of BPH.

Finally, Lilly's argument is contrary to the vast academic literature. In his article "The Assessment of Medical Treatment for Benign Prostatic Hyperplasia (BPH)," Dr. Roehrborn himself discusses various medical treatments of BPH. Ex. 16, Roehrborn 1994. Long before Dr. Roehrborn was a paid Lilly expert in this case, he said treating BPH includes treatments that shrink the prostate (5ARIs) and those that do not (alpha receptor blocking drugs). *Id*. at 181, 186.[3] Physicians understand BPH treatments to include treatment of the symptoms of BPH. *See also*, Ex. 17, McConnell 2003 at 2387 ("Benign prostatic hyperplasia is commonly treated with alpha-adrenergic-receptor antagonists (alpha-blockers) or 5α-reductase inhibitors.").
Lilly's expert cites the literature to highlight that alpha-blockers focus on treating BPH symptoms. *See, e.g.*, Ex. 10, Roehrborn Rebuttal Rep. ¶ 19 n.6. But the articles admit that alpha-blockers treat BPH. For example, Dr. Roehrborn cites "The Emerging Role of Alpha Antagonists in the Therapy of Benign Prostatic Hyperplasia." Ex. 18, Lepor 1991. Even setting aside that the *title* says alpha blockers treat BPH, the article goes on to reference "the rationale for using alpha blockade to treat [BPH]" and that "clinical trials have confirmed the efficacy of alpha blockade in the treatment of BPH." *Id*. at 389. Contrary to its litigation-inspired understanding of "treatment," Lilly knows that treating BPH symptoms is a way to treat BPH.

[3] In his report, Dr. Roehrborn admits that "in common clinical and regulatory language the term 'treatment of BPH' may be used" to describe treatment of LUTS. Ex. 9, Roehrborn Rep. ¶ 81.

2. Tadalafil is an inhibitor of PDE5.

A selective PDE5 inhibitor is "at least 20 times more effective in inhibiting that specific PDE as compared to all other specific PDEs." Order 10/21/16 (Dkt. 149) at 27. Tadalafil meets this definition. The Cialis label states that tadalafil is "a selective inhibitor of cyclic guanosine monophosphate (cGMP)-specific phosphodiesterase type 5 (PDE5)." Ex. 6, Cialis label at 11. As to selectivity, the label specifies that tadalafil is more than 10,000-fold more potent for PDE5 than for PDE1-PDE4. Ex. 6, Cialis label at 12.

Lilly argues that tadalafil is not "selective" under the Court's claim construction because it is not 20 times more selective for PDE5 than for PDE11A1. *See* Ex. 19, Lilly's Third Am. Resp. to Interrogatories at 15; Ex. 20, Rotella Rep. ¶ 135. Lilly's argument fails for three reasons. First, this Court's selectivity requirement must be measured against the five PDEs discussed in the patent and the prosecution history: PDE1 – PDE5. Second, Lilly's understanding of "selectivity" means no compound disclosed in the patent is selective, and such a construction is presumptively incorrect. Third, Lilly cannot argue non-infringement based on a test for selectivity over PDE11, which had not even been discovered at the time of the invention.

a) The Specification and File History Only Discuss PDE1 – PDE5

The selectivity requirement is based on an amendment made during the prosecution of the '061 patent. Order 10/21/16 (Dkt. 149) at 24-27. The applicants there distinguished the "compounds of the currently pending claims [that] are selective inhibitors of PDE IV and/or PDE V" from compounds disclosed in Heiker, U.S. Patent No. 5,721,238, that did "not predictably possess selective inhibitory PDE V and/or PDE IV activity." Ex. 21, '061 File History, March 7, 2010 Amendment at 11. As reflected in the following chart, and as the applicants explained, the

Heiker compounds "shown to possess PDE V inhibitory activity also possess PDE I and/or PDE II inhibitory activity." *Id.* at 12.

Inhibition of the phosphodiesterases in vitro

Example No.	PDE I IC_{50} [mM]	PDE II IC_{50} [mM]	PDE V IC_{50} [mM]
14	5	5	3
15	3	5	
16		5	5
20	10	2	5
29		0.5	1

Heiker '238, col. 10, ll. 7-17. This Court held that the limitation to selective PDE5 inhibitors "was included" in the '124 patent "through the earlier disclaimer and amendment." Order 10/21/16 (Dkt. 149) at 26. The relevant portion of the '061 patent's file history says nothing about selectivity over PDEs 6-11. The only PDEs which the Heiker compounds also inhibited were PDEs 1 and 2.

Further, compounds addressed in the '061 patent would not meet Lilly's version of the selectivity requirement – which requires selectivity vis-à-vis PDEs not mentioned in the patent or the prosecution history. *See* Ex. 20, Rotella Rep. ¶¶ 124-28. Thus, under Lilly's interpretation, the selectivity requirement that was born out of the '061 patent would exclude the compounds disclosed in the '061 patent. Lilly offers nothing to support such a surprising conclusion.

The '124 patent was concerned only with PDEs 1-5, stating that "there is further known the distinction of a number of subesterases of PDE, the ***specific*** phosphodiesterases (sPDE). There is distinguished between ***five different sPDEs*** which are differently distributed in the individual organs . . . ." col. 1, ll. 58-63 (emphasis added). The Court's order setting forth the selectivity requirement mirrors the specification, stating that "a selective inhibitor of ***a specific PDE***" is a compound that is "at least 20 times more effective in inhibiting that ***specific*** PDE as

compared to all other ***specific*** PDEs." Order 10/21/16 (Dkt. 149) at 27 (emphasis added). The Court's claim construction thus limits the '124 patent's coverage to compounds that are at least 20 times more selective for PDE5 than the other specific PDEs identified in the patent, PDE1 – PDE4.

The patent's focus on PDEs 1-5 reflects the state of the art at the time of the invention. Only two other PDEs were known at the time of the invention: PDE6 and PDE7. *See* Ex. 2, Beavo 1 Rep. ¶ 15 (seven PDEs were known at the time of the invention); Ex. 3, Beavo Responsive Rep. ¶ 9. Neither were relevant to the invention. PDE6 was known only to be in the retina (not the prostate), and PDE7 had not yet been identified as present in any specific human tissue. *See* Ex. 4, Bell Rep. ¶¶ 17-18; Ex. 5, Beavo 1995 at 740. On the other hand, PDEs 1-4 were well known to be physiologically relevant in numerous tissues in July 1997, and the field was heavily concentrated on those four PDEs. *See* Ex. 4, Bell Rep. ¶¶ 19-21. Further, it was thought at the time that all PDE5 inhibitors also inhibited PDE6, as there had not been a report of any compound highly selective for PDE5 over PDE6. *See* Ex. 4, Bell Rep. ¶ 21; Ex. 22, Sybertz 1997 at 633. Thus, when the '124 patent and prosecution history describe selective PDE5 inhibitors, it means compounds selective for PDE5 over PDEs 1-4.

b) Lilly's Argument Means No Preferred Embodiments Are Selective

Lilly argues that selective PDE5 inhibitors must be at least 20 times more selective for PDE5 than for all other PDEs. In addition to excluding tadalafil, this argument would also exclude every compound disclosed in the patent. As Lilly's expert notes, none of the compounds disclosed in the patent are 20 times more selective for PDE5 than for PDE6. *See* Ex. 20, Rotella Rep. ¶ 125. On the other hand, four of the compounds disclosed in the patent are 20 times more selective for PDE5 than PDEs 1-4. *See* Ex. 4, Bell Rep. ¶¶ 79-82.

Lilly's argument that tadalafil fails to meet the selectivity requirement depends on an understanding of the claim construction that is presumptively incorrect. *See Arthrex, Inc. v. Smith & Nephew, Inc*., No. 2:15-CV-1047-RSP, 2016 WL 4211504, at *28 (E.D. Tex. Aug. 10, 2016 (rejecting proposed construction "because it would exclude the preferred embodiments") (citing *Vitronics Corp. v. Conceptronic Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996); *Vitronics Corp.*, 90 F.3d 1576 at 1583 (construction where specification's only embodiment falls outside the scope of the patent claim is "rarely, if ever, correct"); *Nellcor Puritan Bennett, Inc. v. Masimo Corp.*, 402 F.3d 1364, 1368 (Fed. Cir. 2005) (construction placing all embodiments outside the scope of the claims is "powerful evidence that the court's construction is incorrect").

c) Lilly Cannot Establish Non-Infringement Based on a Test that was Unavailable at the Time of the Invention

A test can establish non-infringement only if the test is one that "would be employed at the time of the patent application . . . by a person skilled in the art." *Raybestos-Manhattan, Inc. v. Texon, Inc.*, 268 F.2d 839, 842 (1st Cir. 1959); *see also Abbott Labs. v. Alra Labs., Inc.*, No. 92 C 5806, 1997 WL 667796, at *6 (N.D. Ill. Oct. 24, 1997) ("It is well established that a party cannot avoid a finding of infringement by relying on tests not known to the art at the time of the application for the patent or that were not generally used at the time."). This rule is essential because it prevents the patent from "mean[ing] one thing at the time of its issuance and another at some later date upon the discovery of a more accurate test." *Raybestos*, 268 F.2d at 842. The *Raybestos* court for example rejected use of the "Karl Fischer method" to determine the moisture content of a plastic because the defendant failed to show that the test was commonly used in the art. *Id*. The *Abbott Labs* court likewise rejected use of "single crystal x-ray diffraction to determine the structure" of a molecule because there was "no evidence that Abbott or anyone else [in the art] successfully utilized" the technique at the time of the patent application. *Abbott*

Labs., 1997 WL 667796 at *7. *See also Krippelz v. Ford Motor Co.*, 750 F. Supp. 2d 938, 955 (N.D. IL 2010), *rev'd on other grounds* 667 F.3d 1261 (Fed. Cir. 2012) (rejecting non-infringement test not generally used at the time of the invention); ***E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.***, 656 F. Supp. 1343, 1384 (D. Del. 1987), *rev'd on other grounds* 849 F.2d 1430 (Fed. Cir. 1988) (rejecting use of tests to show comonomer content).

In this case, Lilly seeks to prove non-infringement based on tests showing that tadalafil is only 14 times more potent for PDE5 than for PDE11A1. *See* Ex. 23, Rotella Responsive Rep. ¶ 48; Ex. 6, Cialis Label at 12. Lilly's expert concedes that PDE11A1 had not been discovered at the time of the invention. *See* Ex. 2, Beavo 1 Rep. ¶¶ 15-17. Thus, there was no test available at the time that could have supported Lilly's non-infringement position, let alone a test that was commonly used by those of skill in the art as required by *Raybestos* and its progeny. And while PDE7 was known at the time, no test existed that could measure whether a compound was selective for PDE5 over PDE7. *See* Ex. 4, Bell Rep. ¶ 23. The patent's selectivity requirement is thus limited to selectivity regarding the five PDEs discussed in the patent, PDEs 1-5.

3. Prescribing or taking Cialis for BPH comprises direct infringement

Cialis is "administer[ed] to a person in need thereof [in] an effective amount." The Court construed "administering" to mean "providing treatment" and includes both "personally causing that course of action to be carried out" and "directing or supervising the treatment" as well as directing "the decision to use the drug." 8/11/16 Order (Dkt. 131) at 7. Under this construction, physicians prescribing Cialis are administering the treatment by directing the treatment to the patient. Ex. 7, Sliwinski Rep. ¶ 50. And patients administer Cialis by "personally causing the course of action to be carried out."

The Court found that the terms "a person in need thereof" and "effective amount" were sufficiently clear and did not need construction. 8/11/16 Order (Dkt. 131) at 7. A BPH patient taking Cialis is a person in need thereof, and the 5mg dose of Cialis is effective for BPH and for ED + BPH. Ex. 7, Sliwinski Rep. ¶ 50. Prescribing or taking Cialis for BPH directly infringes.

Finally, Cialis is administered in unit dose form, specifically the 5mg dose prescribed by doctors. *Id*. at ¶ 51. The tadalafil compound is also administered in combination with pharmacologically acceptable excipients (e.g., croscarmellose sodium). *Id*. at ¶ 35. Administration of Cialis thus also infringes dependent claim 3 of the '124 patent, which claims the "method of claim 1 wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form." Ex. 1, '124 Pat. at claim 3.

IV. Induced Infringement

The bulk of Lilly's liability in this case stems from Lilly inducing doctors and patients to administer Cialis for treatment of BPH. The Patent Act states that "[w]hoever actively induces infringement of a patent shall be liable as an infringer." 34 U.S.C. § 271(b). To be liable for inducing infringement, a defendant must take some "active steps . . . to encourage direct infringement." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1059 (Fed. Cir. 2010) (quoting *Metro–Goldwyn–Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005)). In addition, the Supreme Court has held "that induced infringement under § 271(b) requires knowledge that the induced acts constitute patent infringement." *Global-Tech Appliances, Inc. v. SEB S.A.*, 563 U.S. 754, 766 (2011). The requisite knowledge may "be inferred from circumstantial evidence." *Warsaw Orthopedic, Inc. v. NuVasive, Inc.*, 824 F.3d 1344, 1347 (Fed. Cir. 2016).

UroPep informed Lilly of the '124 patent, and that Lilly's sale of Cialis for BPH appeared to infringe that patent, in a letter dated October 9, 2014. *See* Ex. 8, Oct. 9, 2014 Notice

Letter. Lilly concedes that it received this letter from UroPep on or around October 9, 2014. *See* Ex. 19, Lilly's Third Am. Resp. to Interrogatories at 22.

Even after acquiring knowledge of the '124 patent, Lilly took active steps to encourage others to infringe the patent. For example, the Cialis label has consistently featured the BPH indication. *See* Ex. 6, Cialis Label at 1, 2. Describing an infringing use in a pharmaceutical label is powerful evidence that Lilly intended others to infringe the '124 patent. *See AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010) (plaintiff "will likely prove induced infringement at trial" where the "proposed label instructs users to perform the patented method"); *Eli Lilly and Co. v. Actavis Elizabeth LLC*, 435 Fed. Appx. 917, 927 (Fed. Cir. 2011) ("the provision of atomoxetine labeled solely for use to treat ADHD constitutes inducement to infringe" Lilly's patent).

Similarly, Lilly's ads for Cialis have consistently featured the BPH indication. The iSpot platform tracks the television ads that Lilly has run for Cialis since July 2012. *See* Knobloch Decl. ¶ 3. Every Cialis television advertisement available on iSpot.tv features the BPH indication. *Id*. at ¶¶ 3-5. These advertisements demonstrate a clear intent to encourage others to infringe the '124 patent. As Lilly itself has noted in other court filings, "[i]t is well-established that intent to induce infringement can be based on marketing literature or package inserts." Ex. 24, Lilly Fed. Cir. Reply Br. in *Eli Lilly v. Actavis*, No. 2010-1500 (Fed. Cir. Sept. 29, 2010). In this case, the marketing, the marketing literature, and the package inserts establish Lilly's intent to induce infringement.

CONCLUSION

For the foregoing reasons, summary judgment of infringement should be granted.

Date: January 17, 2017

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned certifies that the foregoing document was filed electronically in compliance with Local Rule CV-5(a) on January 17, 2017. As such, this document was served on all counsel who are deemed to have consented to electronic service. Local Rule CV-5(a)(3)(A).

Date: January 17, 2017

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